REMARKS

I. Introduction

The Office Action dated June 6, 2008 has been carefully considered. Further and favorable reconsideration is respectfully requested in light of the present amendments and the following remarks.

II. Status of the Claims

Claims 1-39 are pending. Claim 24 is amended to correct a grammatical error. Claim 28 is amended to recite that the mass spectrometer is a tandem mass spectrometer configured to concurrently detect at least two antiretroviral drugs from at least two classes of antiretroviral drugs. Support for this amendment can be found, *inter alia*, in paragraphs [0045-0048] and [0061-0065] of the specification. Claims 33 and 35 are amended to recite that the method does not include any evaporation or reconstitution steps. Support for this amendment can be found, *inter alia*, in paragraph [0043] of the specification. Claim 38 is amended to recite that the sample is deproteinated. Support for this amendment can be found, *inter alia*, in paragraph [0014].

III. Summary of the Office Action

The citations of the references cited in the Office Action can be found in the Notice of References Cited accompanying the action. In the Office Action, the Examiner objected to claims 31 and 32 as being substantial duplicates of claims 1 and 2. The Examiner rejected claims 1-27, 31-32, 34 and 39 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, and rejected claims 15 and 37 under 35 U.S.C. §112, second

paragraph as indefinite. The Examiner rejected claim 28 under 35 U.S.C. §102(b) as being anticipated by publications by Contin, Jayewardene, Korfmacher, Volosov, Watt and Wong. The Examiner rejected claim 38 under 35 U.S.C. §102(b) as being anticipated by publications by Lynch and Hamilton. The Examiner rejected claims 33 and 35-37 under 35 U.S.C. §103(a) as being unpatentable over a publication by Bean. Finally, the Examiner rejected claims 1-39 under 35 U.S.C. §103(a) as being unpatentable over Shoup in view of Bean, Contin Hamilton, Jayewardene, Korfmacher, Lynch, Volosov, Watt or Wong.

IV. Arguments/Remarks

A. Objection of Claims 31 and 32 as Duplicates

Claims 31 and 32 are objected to under 37 C.F.R. 1.75 as being substantial duplicates of claims 1 and 2, if these claims are to be found allowable. Applicant respectfully requests that this objection be held in abeyance as claims 1 and 2 currently stand rejected.

B. Rejection of Claims 1-27, 31-32, 34 and 39 Under 35 U.S.C. §112, First Paragraph

Claims 1-27, 31-32, 34 and 39 currently stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner contends that the phrase "wherein the method does not include any evaporation and reconstitution steps," is not described in the specification. Applicant respectfully traverses the written description rejection.

In paragraphs [0043] and [0059] of the specification, Applicant describes example sample preparations whereby a sample is deproteinated by addition of acetonitrile, followed by subsequent vortexing and centrifugation. The centrifugation supernatant is then transferred directly to a vial for injection into the liquid chromatography – tandem mass spectrometry (LC-MS/MS) system. No evaporation or reconstitution steps are described in this sample preparation process, as the sample is never dried. As such, a method wherein evaporation and reconstitution are not included is clearly described, *inter alia*, in paragraphs [0043] and [0059] of the specification. Reconsideration and withdrawal of the 35 U.S.C. §112, first paragraph, rejection are respectfully requested.

C. Rejection of Claims 15 and 37 Under 35 U.S.C. §112, Second Paragraph

Claims 15 and 37 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite for failing to distinctly claim the subject matter regarded as the invention. Specifically, the Examiner rejects the use of trademarked names. Applicant respectfully traverses the indefiniteness rejection.

M.P.E.P §6081.(v)(I) states that "if the product to which the trademark refers is set forth in such language that its identity is clear, the examiners are authorized to permit the use of the trademark." Applicant respectfully contends that the trademarked spectrometers and molecular weight cut-off filters required by claims 15 and 37 are clearly identifiable for the purposes of these claims. Regarding claim 15, the API 2000, 3000 and 4000 mass spectrometers are each specific spectrometers whose characteristics are well known to those of skill in the art in the

field. In many of the publications cited by the Examiner, a mass spectrometer is described by its trademarked name, without listing further descriptive details. See, for Example, page 311 of Jayewardene at the top of column 1. Regarding claim 37, the molecular cut-off filters are likewise well known to those of skill in the art and are typically described in publications using only their trademarked names. Further, both the spectrometers and filters described are typically not sold under the same name after modification, as manufacturers want consumers to know that the product is now different from its predecessor, hence the series of API names, i.e. API 2000, 3000 and 4000. One of skill in the art would know the specific components being required by claims 15 and 37 within the context of those claims. Finally, regarding the Examiner's concern that the claims would cover someone who has modified their spectrometer, as these claims are method claims, they are only relevant to a person's use of a spectrometer. As such, the claims are not indefinite. Reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph, rejection are respectfully requested.

D. Rejection of Claim 28 under 35 U.S.C. §102(b) as Anticipated

Claim 28 stands rejected under 35 U.S.C. §102(b) as anticipated by Contin, Jayewardene, Korfmacher, Volosov, Watt and Wong. Applicant respectfully traverses the anticipation rejection.

Claim 28, as currently presented, recites a system comprising a tandem mass spectrometer configured to concurrently detect at least two antiretroviral drugs from at least two

classes of antiretroviral drugs. None of the references cited by the Examiner teach all of the limitations of claim 28.

Regarding the references, Contin teaches determination of an anti-epileptic drug using high-performance liquid chromatography (HPLC) and a single mass spectrometer. See, the abstract of Contin. Jayewardene teaches an LC-MS/MS system for the detection of a single protease inhibitor, indinavir. See, the abstract of Jayewardene. Korfmacher teaches an LC-MS/MS assay for detection of new chemical entities, not known drug compounds. See, the abstract of Korfmacher and Table 1. Volosov teaches an LC-MS/MS assay for detection of immunosuppressants. See the abstract of Volosov. Watt teaches an high throughput method where samples are injected one at a time. See, Watt, page 982, column 2. Further, Watt teaches detection of only three drug compounds, L-775,606, indicated for migranes, and imipramine and fluoxetine, both antidepressants. Finally, Wong teaches a liquid chromatography – single mass spectrometer method for the detection of a carbonic anhydrase inhibitor. See, the abstract of Wong.

None of the references teach all of the recitations of claim 28, as currently presented. As such, none of the references can anticipate this claim. Reconsideration and withdrawal of the 35 U.S.C. §102(b) rejections are respectfully requested.

E. Rejection of Claim 38 under 35 U.S.C. §102(b) as Anticipated

Claim 38 stands rejected under 35 U.S.C. §102(b) as anticipated by Lynch and Hamilton. Applicant respectfully traverses the anticipation rejection.

Claim 38 currently recites a method for analysis of a sample comprising or suspected of comprising tenofivir using a mass spectrometer, wherein the sample is deproteinated. Lynch teaches direct injection after lysis of cells. See, Lynch, page 1417, third paragraph. Hamilton also does not teach deproteination. Neither of the cited references teach all of the limitations of claim 38, as currently presented. As such, the cited references cannot anticipate the claim. Reconsideration and withdrawal of the 35 U.S.C. §102(b) rejections are respectfully requested.

F. Rejection of Claim 33 and 35-37 under 35 U.S.C. §103(a) as Obvious

Claims 33 and 35-37 stand rejected under 35 U.S.C. §103(a) as obvious over Bean in view of the teaching of commercially available molecular weight cut-off filters in paragraph [0070] of the specification. Applicant respectfully traverses the obviousness rejection.

Bean teaches therapeutic drug monitoring of antiretroviral drugs using more than one mass spectrometer. The different mass spectrometers are needed for different classes of antiretroviral drugs. See Bean, page 22, second column, first paragraph. Further, Bean only teaches solid-phase extraction and liquid-liquid extraction of samples, wherein the evaporated residues must be reconstituted. See Bean, page 22, second column, first full paragraph. As such, one of skill in the art would not have been able to modify the teachings of Bean using the teachings of the present specification to arrive at the subject matter of claims 33 and 35-37. Accordingly, these claims are not obvious over the teachings of Bean. Reconsideration and withdrawal of the 35 U.S.C. §103(a) rejection are respectfully requested.

G. Rejection of Claims 1-39 under 35 U.S.C. §103(a) as Obvious

Claims 1-39 stand rejected under 35 U.S.C. §103(a) as obvious over Shoup in view of Bean, Contin, Hamilton, Jayewardene, Korfmacher, Lynch, Volosov, Watt or Wong. Applicant respectfully traverses the obviousness rejection.

The currently presented independent claims 1, 28, 29, and 31 recite methods, systems and kits for the analysis of a sample containing at least two antiretroviral drugs from at least two classes of antiretroviral drugs. Currently presented independent claims 33 and 35 recite methods for mass spectrometric analysis of free antiretroviral drug. Currently presented independent claim 38 recites a method for mass spectrometric analysis of a sample comprising or suspected of comprising tenofovir. One of skill in the art would not have looked to Shoup to form any of the inventions recited in these independent claims or the claims that depend from them.

Regarding claims 1, 28, 29 and 31, Shoup expressly teaches away from the analysis of at least two antiretroviral drugs from at least two classes of antiretroviral drugs. On page 17, in the third column, Shoup states:

> Although the initial intention was to measure all of the compounds in a single injection, better quality results were obtained for nelfinavir and nelfinavir M8 metabolite by using the same column and ionization mode with a lower pH mobile phase. Due to concomitant retention time changes, the group of six analytes was best measured using two mobile phases.

The different mobile phases required for the separate injections are shown on page 21 of Shoup. As Shoup does not teach single step analysis of a sample comprising at least two

antiretroviral drugs from at least two classes of antiretroviral drugs, one of skill in the art would not have looked to Shoup. None of the other cited references overcome this deficiency in Shoup.

Regarding claims 33 and 35, Shoup does not provide any teaching or suggestion of analysis of free antiretroviral drug concentration. As is described above, there is nothing in any of the cited secondary references that overcomes this deficiency in a way that would allow for one of skill in the art to arrive at the invention recited in these claims.

Regarding claim 38, Shoup does not provide a teaching or suggestion of the analysis of tenofovir, a nucleotide analog reverse transcriptase inhibitor. Instead, Shoup provides a teaching of a delavirdine, a non-nucleoside reverse transcriptase inhibitor, a completely different class of antiretroviral drug. As Shoup itself recognizes, different antiretroviral drugs, including different drugs in the same class, can be difficult to analyze using a single system. As such, one of skill in the art would not have looked to Shoup for guidance relating to the analysis of tenofivir. There is nothing in Hamilton or Lynch that overcomes this deficiency.

Accordingly, one of skill in the art would not have found it obvious to combine Shoup with any of the cited secondary references to arrive at the subject matter of current claims 1-39. Reconsideration and withdrawal of the 35 U.S.C. §103(a) rejections are respectfully requested.

V. Conclusion

All rejections set forth in the Office Action have been addressed with the arguments and amendments above. In the event there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that the prosecution of this application may be expedited.

Please charge any shortage or credit any overpayment of fees to BLANK ROME LLP, Deposit Account No. 23-2185 (130866.0109). In the event that a petition for an extension of time is required to be submitted herewith and in the event that a separate petition does not accompany this response, Applicant hereby petitions under 37 CFR 1.136(a) for an extension of time for as many months as are required to render this submission timely. Any fee due is authorized above.

Respectfully submitted,

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